Remarks/Arguments

The foregoing amendments to the claims are of a formal nature, and do not add new matter. Claims 119-138 were pending in this application and were rejected on various grounds. Claims 127-128 and 132-134 are canceled without prejudice or disclaimer. Claims 119-123 have been amended to recite "wherein said nucleic acid is amplified in colon tumors". Claims 139-142 have been added, support for which is found in canceled claim 132 and in the instant specification at page 285, line 11 onwards. Thus, Claims 119-126, 129-131 and 135-142 are pending in this application. The rejections to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the gene amplification assay for patentable utility which was first disclosed in U.S. Provisional Application 60/141037, filed June 23, 1999, priority to which has been claimed in this application. Hence, the present application is entitled to at least the priority date of **June 23, 1999.**

Information Disclosure Statement

Applicants submit an IDS separately enlisting references recited in the Blast report in order to be compliant with 37 C.F.R. § 1.98(a)(1). Consideration of this Information Disclosure Statement is respectfully requested.

Specification

A. The disclosure was objected to by the Examiner as containing "embedded hyperlink and/or other form of browser-executable code." The foregoing amendment to the specification which deleted all embedded hyperlinks, is believed to overcome the present objections.

B. The title of the invention has been amended to better describe the claimed invention.

Accordingly, Applicants believe that all objections to the specification have been overcome and should be withdrawn.

Claim Objections

The syntax of claims 119-131 was objected to for referring to 'Figures' in the claim language. Accordingly, Applicants have amended the claims to delete such references and thus this objection should be withdrawn.

Claim Rejections – 35 USC § 101 and §112, 1st paragraph

Claims 119-138 are rejected under 35 U.S.C. §101 allegedly because "the claimed invention is not supported by a specific, substantial and credible asserted utility or a well established utility. These claims are directed to polynucleotides having various sequence homology to SEQ ID NO: 325 or encoding SEQ ID NO: 326." Claims 119-138 are further rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention". Applicants respectfully disagree with and traverse these rejections.

The Examiner asserts that since the encoding polynucleotides, vectors, host cells and methods of making the protein also lacks utility.

Utility Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must

be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.** Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

Arguments

As discussed under the section on "priority", Applicants rely on the gene amplification data for patentable utility for the PRO1281 gene and polynucleotides encoding the PRO1281 protein, which was first disclosed in U.S. Provisional Application 60/141037, filed June 23, 1999, and hence, the present application is at least entitled to the filing date of **June 23, 1999.** Applicants further submit that the gene amplification data establish patentable utility, for reasons discussed below.

Gene amplification is an essential mechanism for oncogene activation and the assay is well-described in Example 170, page 539 of the present application. The gene amplification data shows that genomic DNA was isolated from a variety of primary cancers and cancer cell lines listed in Table 9 (especially page 554, Table 9C) which includes primary colon cancers of the type and stage indicated in Table 8 (page 546). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 539, lines 27-29). Gene amplification was monitored using real-time quantitative TaqMan™ PCR and the results are set forth in Table 9A. As explained in the passage on page 539, lines 37-39, "the results of TaqMan™ PCR are reported in ΔCt units. **One unit** corresponds to one PCR cycle or approximately a **2-fold amplification**, relative to control, two units correspond to 4-fold, 3 units to 8-fold amplification and so on" (emphasis added). Table 9C indicates that PRO1281 showed approximately 1.07-1.15 ΔCt units which corresponds to $2^{1.07}$-$2^{1.15}$- fold amplification or **2.099 fold to 2.219 -fold** amplification in colon tumors which is significant and thus, the PRO1281 gene has utility as a diagnostic marker of human colon cancer.

Applicants further submit that, since the pending claims in the instant application are drawn to nucleic acids that encode PRO1281, not polypeptides, any rejections directed to polypeptides are misplaced in this case. Further, in view of the functional recitation added to the instant claims, claims are directed to naturally occurring degenerate nucleic acids that encode PRO1281 that are amplified in colon cancer. Thus, these PRO1281 nucleic acids have utility in the diagnosis of colon cancer and based on the above discussions, one skilled in the art would know how to use the claimed nucleic acids at the time the application was filed.

Thus, these rejections under 35 U.S.C. §101 and §112, first paragraph should be withdrawn.

Claim Rejections - 35 USC § 112, first paragraph-enablement

B. Claims 119-138 are also rejected under 35 U.S.C. §112, first paragraph as containing subject matter not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. The Examiner noted that for the biological deposit ATCC 203129, Applicants need to provide a declaration containing (1) the current ATCC address; and (2) a statement stating that all restrictions imposed by the depositor on the availability of

deposited material to the public will be irrevocably removed upon the granting of the patent.

Applicants submit that amendments to the specification have (1) the current ATCC address; and (2) incorporated the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent." Thus, this rejection should be withdrawn.

C. Further, the Office action asserts that Claims 119-138 would still be rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for SEQ ID NO: 325 and 326, does not reasonably provide enablement for polynucleotides or polypeptides having at least 80%, 85%, 90%, 95% or 99% sequence identity to SEQ ID NO:325 or 326, to the protein encoded by ATCC No. 203129, for the extracellular domain thereof, or for vectors and host cells containing these polynucleotides. The Examiner also noted that the claims are broad because the claims have no functional limitation and hence, asserts that it would require undue experimentation to use the invention commensurate in scope with the claims.

Firstly, in view of the deletion of references to the "extracellular domain" in the claims, these rejections are obviated. Further, claims have been amended to include a functional recitation "wherein said nucleic acid is amplified in colon tumors." Based on the utility for PRO1281 gene and the nucleic acids encoding the polypeptides in the diagnosis of colon cancer, as discussed above, Applicants submit that the skilled artisan would not require undue experimentation to make and use the claimed invention.

Accordingly, Applicants request that this rejection be withdrawn.

Claim Rejections - 35 USC § 112, first paragraph-written description

Claims 119-138 are also rejected under 35 U.S.C. 112, first paragraph because, according to Examiner, the subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing".

Without acquiescing to the propriety of this rejection, Applicants have amended claims 119-123 to recite a functional recitation: "wherein the nucleic acid encoding said polypeptide is amplified in colon tumors." Claims 127-128, 132-134 have been canceled without prejudice or

disclaimer and hence this rejection is moot with respect to these claims. Applicants respectfully traverse this rejection to the remaining pending claims.

The Legal standard for Written Description

The well- established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is whether the disclosure "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *In re* Kaslow, 707 F.2d 1366, 1375, 212 USPQ 1089, 1096 (Fed. Cir. 1983); see also Vas-Cath, Inc. v. Mahurkar, 935 F. 2d at 1563, 19 USPQ2d at 1116 (Fed. cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. see e.g.Vas-Cath, Inc. v. Mahurkar, 935 F. 2d at 1563, 19 USPQ2d at 1116 (Fed. cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. Union Oil v. Atlantic Richfield Co., 208 F. 3d 989, 996 (Fed. Cir. 2000).

Arguments

As noted above, whether the Applicants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including the level of knowledge and skill in the art, and the teaching provided by the specification. The inventor is not required to describe every single detail of his/her invention. An Applicant's disclosure obligation varies according to the art to which the invention pertains.

The present invention pertains to the field of recombinant DNA/protein technology. It is well established that the level of skill in this field is very high since a representative person of skill is generally a Ph.D. scientist with several years of experience. Accordingly, the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made. The instant invention, defined by the claims, concerns polypeptides having 80%, 85%, 90%, 95% or 99% sequence identity with the disclosed polypeptide sequence SEQ ID NO: 326 and further, with the functional recitation: "wherein the nucleic acid encoding said polypeptide is amplified in lung and colon tumors." Based on the

detailed description of the cloning and expression of variants of PRO1281 in the specification, the description of the gene amplification assay and description of testing the ability of test variant polypeptides in the assay, the actual reduction to practice of sequence SEQ ID NO: 326 and the functional recitation in the instant claims, Applicants submit that one of skilled in the art would know that Applicants possessed the invention as claimed in the instant claims.

Hence, Applicants submit that this rejection should be withdrawn.

Claim Rejections – 35 USC § 112, second paragraph

Claims 119-138 were rejected under 35 U.S.C. §112, second paragraph for being indefinite.

A. The Examiner alleges that the protein identified as PRO1281 is disclosed as a soluble protein (protease)and accordingly, claims that recite an "extracellular domain" is indefinite as the art does not recognize soluble proteins as having such domains.

Without acquiescing to the propriety of this rejection, merely to expedite prosecution in this case, Applicants have deleted any reference to "extracellular domains" in the pending claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

B. Claims 132-134 were rejected as vague and indefinite for reciting the term "hybridizes" without reciting any conditions or reciting "stringent conditions" wherein these conditions are not known.

Without acquiescing to the propriety of this rejection, merely to expedite prosecution in this case, Applicants have deleted claims 132-134 and hence this rejection is moot with respect to these claims. Applicants respectfully traverse this rejection as applied to new claims 139-142.

Claims 139-142 recite the precise conditions under which hybridization was done and hence, these claims are not indefinite. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claim Rejections - 35 USC § 102

Claims 119-138 were rejected under 35 U.S.C. §102(b) as being anticipated by Baker *et al.* (WO99/63088) published December 1999.

Applicants have made a proper assertion of priority based on U.S. Provisional Application 60/141037, filed **June 23, 1999** for this application and believe they are entitled to this date based on the discussions above. Accordingly, Applicants submit that Baker *et al.* is not prior art and hence, this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C60). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: June 7, 2004

Daphne Reddy

Daphne Reddy
Reg. No. 53,507

HELLER EHRMAN WHITE & McAULIFFE LLP
Customer No. 35489
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

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